

Notice of Allowability

Application No.

09/841,744

Examiner

Chih-Min Kam

Applicant(s)

DIMARTINO, JORGE F.

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 12/15/04.
2. ☒ The allowed claim(s) is/are 1,4,13,14,16-28 and 30.
3. ☒ The drawings filed on 24 April 2001 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date 4/28/04
4. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413),
Paper No./Mail Date 20041019;20050128.
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

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An **Examiner's Amendment** to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Maya Skubatch on January 27, 2005.

Examiner's Amendments to the Specification:

Please amend the paragraph starting at page 8, line 27 as follows:

Examples of hydroxamic acids and hydroxamic acid derivatives include, but are not limited to, trichostatin A (TSA), suberoylanilide hydroxamic acid (SAHA), oxamflatin, suberic bishydroxamic acid (SBHA), m-carboxy-cinnamic acid bishydroxamic acid (CBHA), and pyroxamide. Examples of cyclic peptides include, but are not limited to, trapoxin A, apicidin and FR901228. Examples of benzamides include but are not limited to MS-27-275 (N-(2-aminophenyl)-4-[N-(pyridin-3-ylmethoxycarbonyl)aminomethyl]benzamide). ~~Examples~~ Examples of short-chain fatty acids include but are not limited to butyrates (e.g., butyric acid and phenylbutyrate (PB)).

Examiner's Amendments to the Claims:

Claim 1 has been amended as follows:

1. (Currently amended) A method for treating a patient having a cancer with a combination therapy, comprising:

administering to said patient a therapeutically effective amount of a DNA methylation inhibitor that is 5-azacytidine or decitabine at a dose ranging from 1 to 50 mg/m² per day, in combination with a therapeutically effective amount of a histone deacetylase inhibitor selected from the group consisting of trichostatin A, suberoylanilide

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hydroxamic acid, oxamflatin, suberic bishydroxamic acid, m-carboxy-cinnamic acid bishydroxamic acid, pyroxamide, trapoxin A, apicidin, depsipeptide, N-(2-aminophenyl)-4-[N-(pyridin-3-ylmethoxycarbonyl)aminomethyl]benzamide, butyric acid, phenylbutyrate and arginine butyrate.

The following is an **Examiner's Statement of Reasons for Allowance**: The following references appear to be the closest art to the claimed invention. Santini *et al.* (Annals of Internal Medicine, 134, 573-586 (April 3, 2001)) teach various cancers including solid tumors, malignant hematological diseases, myelodysplastic syndromes, and chronic myelogenous leukemia are treated with different doses of a DNA methylation inhibitor, decitabine or 5-azacytidine, one example indicates elderly patients with high risk myelodysplastic syndrome were treated with decitabine at a dosage within the range of 1-50 mg/m². Cameron *et al.* (Nature Genetics 21, 103-107 (January 1999)) disclose several tumor suppressor genes, which are hypermethylated genes and silenced in the cancer cells, are re-expressed in the presence of low dose 5-aza-2'-deoxycytidine and trichostatin A. Zhu *et al.* (Cancer Research 61, 1327-1333 (February 15, 2001)) teach HDA inhibitors, depsipeptide (FR901228) and trichostatin A induce apoptotic cell death of human lung cancer cells, and this induced apoptosis is greatly enhanced in the presence of the DNA methylation inhibitor, 5-aza-2'-deoxycytidine. Thus, it appears that the combined references of Santini *et al.* with Cameron *et al.* or Zhu *et al.* teach the claimed invention. However, a declaration under 37 C.F.R. 1.131 filed December 15, 2004 by applicants indicate the invention of the instant application was conceived prior to April 3, 2001, the publication date of Santini *et al.*, and this conception was coupled with diligence during the period between the publication date of Santini *et al.*, April 3, 2001 and the filing of the instant patent application April 24, 2001. Therefore, the rejection under 35 USC 103(a) was withdrawn, and the claims are allowable over the art of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

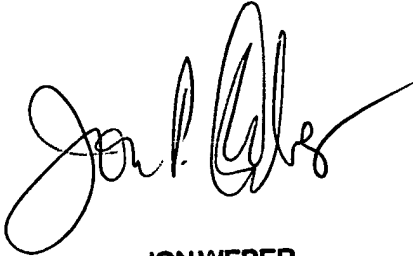
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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D. *CMK*
Patent Examiner

CMK

January 28, 2005



JON WEBER
SUPERVISORY PATENT EXAMINER